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Appraisal

Critically Appraised Papers

High-flow oxygen reduces 90-day mortality, compared with standard oxygen or non-invasive ventilation, in patients with acute hypoxaemic respiratory failure

Synopsis

Summary of: Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *NEJM*. 2015;372:2185-2196.

Question: In patients who have acute hypoxaemic, non-hypercapnic respiratory failure, does high-flow oxygen reduce intubation rates or 90-day mortality compared with non-invasive ventilation or standard oxygen? ***Design:*** Multicentre, randomised, controlled trial with concealed allocation. Participants, therapists and outcome assessors were not blinded, although intubation criteria were determined *a priori* to minimise bias. ***Setting:*** Twenty-three intensive care units in France and Belgium. Exclusion criteria included: exacerbation of asthma/chronic respiratory failure, cardiogenic pulmonary oedema, haemodynamic instability/vasopressors, Glasgow Coma Scale $\leq$ 12 points, contraindications to non-invasive ventilation and urgent need for endotracheal intubation. Randomisation of 313 participants allocated 106 to high-flow oxygen, 111 to non-invasive ventilation and 96 to standard oxygen. ***Interventions:*** The high-flow oxygen group received continuous oxygen therapy through large-bore binasal prongs at 50 l/min. Fraction of inspired oxygen was initiated at 1.0 and adjusted to maintain arterial oxygen saturation $\geq$ 92% (for $\geq$ 2 days). The non-invasive ventilation group received pressure support through a facemask, adjusted to achieve an expired tidal volume of 7 to 10 ml/kg, with initial positive end-expiratory pressure of 2 to 10 cmH_2O (for $\geq$ 8 hours/day for $\geq$ 2 days; parameters were adjusted to maintain arterial oxygen saturation $\geq$ 92%). The standard oxygen group received continuous oxygen through a non-rebreather facemask at $\geq$ 10 l/min (rate adjusted to maintain arterial oxygen saturation $\geq$ 92%). ***Outcome measures:*** The primary outcome was the proportion of participants that was intubated at day 28 (using pre-specified criteria for intubation). Secondary outcomes included all-cause mortality (in intensive care and at 90 days) and ventilator-free days at day 28. ***Results:*** A total of 310 participants were analysed. There were no differences in intubation rates between standard oxygen and high-flow oxygen (OR 1.45, 95% CI 0.83 to 2.55), and non-invasive ventilation and high-flow oxygen (OR 1.65, 95% CI 0.96 to 2.84). Ventilator-free days were higher following high-flow oxygen compared with non-invasive ventilation (mean difference –5.0 days, 95% CI –7.8 to –2.3) but not standard oxygen (mean difference –2.0 days, 95% CI –4.5 to 0.5). Mortality at 90 days was better following high-flow oxygen compared with both standard oxygen (hazard ratio [HR] 2.01, 95% CI 1.01 to 3.99) and non-invasive ventilation (HR 2.50, 95% CI 1.31 to 4.78). ***Conclusion:*** Although treatment with high-flow oxygen, non-invasive ventilation or standard oxygen did not result in different intubation rates, those who were treated with high-flow oxygen had better 90-day mortality.

[Mean differences and 95% CIs for ventilator-free days calculated by the CAP Editor]

Provenance: Invited. Not peer-reviewed.

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Commentary

Non-invasive ventilation is highly effective in reducing intubation and mortality rates in patients with acute hypercapnic respiratory failure.[1] However, evidence of benefit in acute hypoxaemic respiratory failure is less convincing.[2] Additionally, non-invasive ventilation requires skill to implement and optimise.

High-flow oxygen is increasingly being used as an alternative to non-invasive ventilation in managing acute hypoxaemia. This technique is simple to set up and permits a more precise and higher delivery of inspired oxygen than standard oxygen delivery devices. The high gas flow rates that are used also generate low level positive end-expiratory airway pressure, providing physiological benefits including reduced work of breathing, improved ventilation-perfusion matching and increased washout of carbon dioxide in the anatomical dead space. However, whether these benefits extend to improvements in important patient outcomes such as intubation and mortality rates has not previously been studied, despite increasing acceptance as usual care in acute care settings.

While the study of Frat et al is a negative trial with respect to the primary outcome of intubation rate, it provides useful insights into the use of high-flow oxygen and non-invasive ventilation in acute hypoxaemic respiratory failure. Since neither high-flow oxygen nor non-invasive ventilation reduced intubation rates, close monitoring is crucial and intubation is necessary if rapid clinical improvements are not achieved, as delaying escalation of therapy is associated with poorer outcome.[3] The reduced intubation rates amongst those with more severe hypoxaemia allocated to high-flow oxygen is interesting and warrants further investigation. Comfort and reductions in dyspnoea were greater with high-flow oxygen, suggesting that this therapy is a better choice than non-invasive ventilation for palliation of patients with end-stage respiratory failure.

Before the widespread adoption of this technique in respiratory and acute care settings, further well-designed trials such as this are crucial to better define the timing, indications and limitations of high-flow oxygen in respiratory and critical care practice.

Provenance: Invited. Not peer-reviewed.

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